2019-nCoV Literature Situation Report (Lit Rep)
February 10, 2020

Key Takeaways

- **A descriptive study of 1,099 2019-nCoV patients in China offers some of the most robust information about clinical characteristics available.**
- **Mental health of medical staff and the public both in China and other affected countries continue to draw interest in the literature and news media.**
- **Increasingly, researchers are emphasizing the unreliability of case fatality estimates due to underreporting and under-screening in addition to duration of illness. A new report trying to account for some of this bias estimated a case fatality of less than 1% in China, the lowest estimate to date.**

Transmission and Global Spread

- Researchers developed a geo-stratified framework for estimating 2019-nCoV transmission dynamics in China, addressing underreporting and under-screening biases affecting Wuhan case counts. They estimate a basic reproductive number of 3.24 in Wuhan before the lockdown on Jan 23.

  Cao et al. (Feb 9, 2020). Incorporating Human Movement Data to Improve Epidemiological Estimates for 2019-nCoV. Pre Print downloaded Feb 9 from https://www.medrxiv.org/content/10.1101/2020.02.07.20021071v1

- Time between diagnosis and death/recovery in addition to underreporting of cases will have tremendous spatiotemporal variation globally.
  - Wuhan case fatality estimates are likely overestimated due to vast underreporting of mild and asymptomatic cases.
  - Delayed identification of 2019-nCoV deaths outside of Wuhan could mean that case fatality estimated based on non-Wuhan cases underestimate true case fatality.
  - Geographic differences in case fatality could be related to structural factors, like access to health care and the type of health care available.

  Manuel et al. (Feb 7, 2020). 2019-Novel Coronavirus (2019-nCoV): estimating the case fatality rate – a word of caution. Swiss Med Wkly. https://smw.ch/article/doi/smw.2020.20203

- 565 Japanese citizens were evacuated from Wuhan at the end of January and were screened for 2019-nCoV symptoms (63 symptomatic) and tested (8 tested positive by RT-PCR, 5 of whom were asymptomatic).
- Using data from these travelers, researchers estimated the rate of under-ascertainment of cases in Wuhan to be 9.2%. This would suggest a true case fatality far lower than recent estimates, likely closer to 0.3-0.6%.

Nishiura et al. (Feb 4, 2020). The Rate of Underascertainment of Novel Coronavirus (2019-nCoV) Infection: Estimation Using Japanese Passengers Data on Evacuation Flights. J Clin Med. https://doi.org/10.3390/jcm9020419

- Preliminary data suggest that 2019-nCoV may be about 10% less pathogenic than SARS-CoV and about 40% less than MERS-CoV.
- More research is needed to determine of 2019-nCoV has the same mutation and recombination characteristics found in SARS-CoV or if it is more static like MERS-CoV and to identify key routes of infection, which could be *both* respiratory and gastrointestinal.

Chen (Feb 4, 2020). Pathogenicity and Transmissibility of 2019-nCoV—A Quick Overview and Comparison with Other Emerging Viruses. Microbes and Infection. (pre-proof) https://www.sciencedirect.com/science/article/pii/S1286457920300265?via%3Dihub

Modelling and Prediction

- Using clinical, travel history, and disease progression information for 46 2019-nCoV cases who traveled from Wuhan before Jan 23 and were subsequently confirmed elsewhere, researchers attempted to model transmission dynamics with more precision than previous reports by simulating infection time.
- Findings suggest a much higher epidemic growth rate in the early days of the outbreak in Wuhan than previous reports, with a 2.9 day doubling time.

Zhao et al. (Feb 9, 2020). Analysis of the epidemic growth of the early 2019-nCoV outbreak using internationally confirmed cases. Pre Print downloaded Feb 10 from http://dx.doi.org/10.1101/2020.02.06.20020941

Clinical Characteristics and Health Care Setting

- In reviewing the importation of the first 2019-nCoV case to Korea, clinicians call for testing all symptomatic individuals with epidemiologic risk for 2019-nCoV rather than waiting for pneumonia or other symptoms to develop. They describe potential flaws of relying on chest radiography and clinical cues, urging clinicians to prioritize travel history to improve early detection and isolation.

Kim et al. (Feb 10, 2020). The First Case of 2019 Novel Coronavirus Pneumonia Imported into Korea from Wuhan, China: Implication for Infection Prevention and Control Measures. J Korean Med Sci. https://doi.org/10.3346/jkms.2020.35.e61

- Clinical characteristics of 1,099 laboratory-confirmed 2019-nCoV patients at 552 hospitals across China (through Jan 29) are described in relation to disease severity and a composite endpoint of ICU admission, mechanical ventilation, and death. Disease severity (including oxygen saturation, respiratory rate, blood leukocyte/lymphocyte count, and chest X-ray/CT manifestations) predicts clinical outcomes
    - Median age of 47 years (only 9 cases below 15 years old)
    - 41.8% female
    - 1.18% had direct contact with wildlife
    - 31.3% had been to Wuhan; 71.8% had contact with someone who had been to Wuhan
    - Symptoms: Fever (87.9%), cough (67.7%), fatigue (38.1%). Diarrhea, uncommon
    - Median incubation period = 3 days (range 0-24)
    - 76.4% had various chest CT abnormalities

- 79.1% developed pneumonia
  - Median time from symptom onset to pneumonia diagnosis 4 days (range 2-4)
- 1.4% had died at time of publication

Guan et al. (Feb 9, 2020). Clinical characteristics of 2019 novel coronavirus infection in China. Pre Print downloaded Feb 9 from https://www.medrxiv.org/content/10.1101/2020.02.06.20020974v1

- Researchers explain the need for developing serological assays for 2019-nCoV testing. Real-time RT-PCR or next-generation sequencing are the primary methods for confirming 2019-nCoV infection, but with limited supplies, the number of cases that can be tested is restricted and delayed. Researchers propose conventional serological assays as a potential alternative.
- A backlog of tests in China produces artificial jumps in daily case reports.
- Sensitivity and specificity of the predominant testing methods have not been assessed yet.

Xiao et al. (Feb 7, 2020). Evolving status of the 2019 novel coronavirus Infection: proposal of conventional serologic assays for disease diagnosis and infection monitoring. J Med Virology. https://doi.org/10.1002/jmv.25702

- CT imaging for two 2019-nCoV patients demonstrate changes over the duration of disease.

Fang et al. (Feb 7, 2020). CT Manifestations of Two Cases of 2019 Novel Coronavirus (2019-nCoV) Pneumonia. Radiology.
https://pubs.rsna.org/doi/10.1148/radiol.2020200280

- Clinical characteristics of 15 2019-nCoV patients outside of Wuhan are described.

Chang et al. (Feb 7, 2020). Epidemiologic and Clinical Characteristics of Novel Coronavirus Infections Involving 13 Patients Outside Wuhan, China. JAMA Research Letter. https://jamanetwork.com/journals/jama/fullarticle/2761043?resultClick=1

- A Chinese team provides recommendations for addressing 2019-nCoV preparedness and response in neonatology intensive care units based on prior experiences with coronavirus outbreaks.

Wang et al. (Feb 7, 2020). A contingency plan for the management of the 2019 novel coronavirus outbreak in neonatal intensive care units. The Lancet.
https://doi.org/10.1016/S2352-4642(20)30040-7

- Authors conducted a literature review to determine the ability of coronaviruses to persist on inanimate objects, with potential applications for the current 2019-nCoV outbreak. Both SARS and MERS coronaviruses can persist on inanimate surfaces (fomites) for up to 9 days. They can be inactivated effectively by disinfection procedures with 6271% ethanol, 0.5% hydrogen peroxide, or 0.1% sodium hypchlorite within one minute.

Kampf et al. (Feb 6, 2020). Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. J of Hosp Infect.
https://doi.org/10.1016/j.jhin.2020.01.022

- Following WHO rules for guideline development, this team developed rapid advice guidelines for 2019-nCoV that include epidemiologic characteristics along with recommendations for disease screening and population prevention, diagnosis, treatment and control, nosocomial infection prevention and control, and nursing.

- This rich tool includes some specific information from Zhongnan Hospital of Wuhan University.

  Jin et al. (Feb 6, 2020). A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Military Medical Research. https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-0233-6

- Researchers developed two 1-step real-time RT PCR assays for the Sarbecovirus subgenus to account for potential genetic diversity of the 2019-nCoV circulating in humans. Assays were tested on respiratory samples and results are promising. Further testing is needed.
  - Lo and Chiu offer some commentary and critique of this earlier report and opportunities for further testing.

    Chu et al. (Jan 31, 2020). Molecular Diagnosis of a Novel Coronavirus (2019-nCoV) Causing an Outbreak of Pneumonia. Clinical Chemistry.
    https://academic.oup.com/clinchem/advance-article/doi/10.1093/clinchem/hvaa029/5719336

    Lo and Rossa (Feb 7, 2020). Racing towards the development of diagnostics for a novel coronavirus (2019-nCoV). Clinical Chemistry.
    https://academic.oup.com/clinchem/advance-article/doi/10.1093/clinchem/hvaa038/5729988

Virology

- Researchers re-analyzed data reported in two prior papers that suggested snakes are an intermediary host for 2019-nCov. Their results do not support this conclusion, pointing instead to mammals and birds as more likely intermediary hosts. Findings also indicated that the previously reported "unlikely" similarity between a 2019-nCoV spike protein insertion and that of HIV-I was actually the result of natural evolution from bat coronaviruses.

  Zhang et al. (Feb 8, 2020). Protein structure and sequence re-analysis of 2019-nCoV genome does not indicate snakes as its intermediate host or the unique similarity between its spike protein insertions and HIV-I. Pre Print downloaded Feb 10 from https://doi.org/10.1101/2020.02.04.933135

- The 2019-nCoV virus genome has undergone in-depth annotation, and differences between the virus and SARS and SARS-like coronaviruses are described. These differences may explain functional and pathogenic differences between the viruses.

  Wu et al (Feb 7, 2020). Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. Cell Host & Microbe.
  https://doi.org/10.1016/j.chom.2020.02.001

Mental Health and Personal Impact

- Social and economic impacts of the 2019-nCoV outbreak are discussed. They are contextualized within the history of emergencies in the region, including atomic bombings, sarin gas attacks, H1N1, and the Fukushima nuclear accident. Anxiety disorders, PTSD, depression, somatization, lower perceived health, public fear, discrimination, and stigmatization are key highlighted as challenges.

  Shigemura et al. (Feb 8, 2020). Public responses to the novel 2019 coronavirus (2019-nCoV) in Japan: mental health consequences and target populations. Psychiatry and Clinical Neurosciences. https://doi.org/10.1111/pcn.12988

- This commentary describes the difficult conditions and social environment in Beijing, with some emphasis on the experiences of clinical staff at regional hospitals.

  Mowbray (Feb 7, 2020). In Beijing, coronavirus 2019-nCoV has created a siege mentality. BMJ. https://doi.org/10.1136/bmj.m516

- In this commentary, authors discuss the mental health effects experienced by medical workers in Wuhan during the current outbreak and the steps taken by local government and health care facility officials to support them.

  Kang et al. (Feb 5, 2020). The mental health of medical workers in Wuhan, China dealing with the 2019 novel coronavirus. The Lancet. https://doi.org/10.1016/S2215-0366(20)30047-X

In addition to the articles described here, there are several editorials, commentaries, and technical (e.g., drug trial) papers available to view via the 2019-nCoV SharePoint site along with previous Lit Reps.